

agonisms and antagonisms with those proteins, and by comparison with acoustic or electromagnetic phenomena exhibiting distinct series of frequencies for which effects have been observed.

REMARKS

Consideration of this Amendment After Final Rejection is respectfully requested. Claims 1-12 have been cancelled and replaced with new Claims 13-18. These new claims are a translation of the claims that have been recently approved by the European Patent Office – with the exception that a disclaimer at the end of the Claim 1, required by European but not by U. S. law, has been suppressed.

A new declaration in compliance with 37 C.F.R. 1.67 (a) identifying this application by application number and filing date is enclosed.

Rejections Under 35 U.S.C. § 101

Claim 9 was rejected under 35 U.S.C. § 101 and has been cancelled.

Claims 1-8 and 11 were rejected under 35 U.S.C. § 101 because the disclosed invention is inoperative and therefore lacks utility. The Examiner states:

The instant application does not disclose a set of operable parameters for the regulation of protein synthesis by administration of audible sound of any type. Additionally, there is no known principle that would lead one to reasonably believe that the regulation of protein synthesis by the playing of audible music to a subject could occur. *Office Action of 5/25/01, page 6.*

The Examiner relies upon the reasons set forth in the rejection under 35 U.S.C. § 112, first paragraph and further urges that his position is correct, *inter alia*, because the Declaration of Dr. Sternheimer filed in 1999 is not convincing based on three premises: (1) that the date of execution is not fully legible; (2) that the annexes referred to do not describe carefully controlled experiments for all relevant conditions; and (3) none of the annexes or the declaration itself shows any data in connection with the synthesis of any particular protein. *Office Action of 5/25/01, pages 6-7.*

The Examiner's lack of utility rejection under 35 U.S.C. §101 urging that "there is no known principle that would lead one to reasonably believe that the regulation of protein synthesis by the playing of audible music to a subject could occur," is respectfully traversed. The Examiner's opinion appears to be predicated upon Dr. Sternheimer's alleged failure to prove utility with "actual" evidence.

Dr. Sternheimer has reviewed this rejection with aghast as he and others have been using and developing the claimed invention since 1992. Dr. Sternheimer has set forth in the specification, his declaration dated May 19, 1999 (Sternheimer I), and his further views that there is indeed utility of his invention in his second declaration attached hereto. *Declaration of Dr. Joel Sternheimer II dated October 26, 2001*. Before presenting the evidence regarding utility, the Examiner is reminded of the admonition of the Federal Circuit that "statements that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained." *In re Cortright*, 49 USPQ 2d 1464, 1469 (Fed. Cir. 1999) (Also discussing the interplay between 35 U.S.C. §101 and 35 U.S.C. §112, ¶1.).

First, the specification teaches utility of the method for epigenetic regulation of protein biosynthesis *in situ* in Examples 5 and 6 of the *Specification at Pages at 24-28*.

Second, Dr. Sternheimer's first declaration provides the example of Mr. Pedro Ferrandiz to show that the method of the invention allows and controls the *in situ* regulation of the synthesis of selected proteins. *See Declaration of Dr. Sternheimer I dated May 19, 1999 at ¶ 5, Annex 2*.

Third, Dr. Sternheimer in Sternheimer II, notes that in evolved organisms, amino acids are carried through the blood, and are thus subject heartbeat's phase. He discusses the work of Dr. N'guyen Tan-Hon to show that there is direct evidence that this very phase also governs polypeptide elongation. *See Declaration of Dr. Sternheimer II dated October 26, 2001 at ¶ 10*. The subjective evaluation of the protein elongation rhythm which one is able to perform using inventor's method may be checked according to the work of Dr. Tan-Hon and compared to the speed of the elongation process as directly measured. Table I gives those values for a few

common proteins, and Fig. 3 shows the resulting graphs where the phase is clearly visible for every different protein. See, *Declaration of Dr. Sternheimer II dated October 26, 2001 at ¶ 10*.

The Examiner also contends that experiments done are not "controlled." Not only the experiments such as reported in Dr. Fukagawa's book where always compared with controls, but a recent thesis in Gand University has reproduced several of them with all parameters measured, such as moisture and temperature in different parts of the greenhouse, etc. . . In this work, titled "Influence of variable sound frequencies on growth and development of plants," Y. van Doorne has in particular been able to check the function of tomato extensins, by measuring an average differential increase in plant size of 0.5 cm per day in plants exposed 6 minutes per day to extensin proteodies, as compared with controls (see figure page 129 and the 50-page statistical analysis at the end of the thesis, performed thanks to the helping supervision of Prof. J. Cumps): in particular no increase in plant nodes was observed, as expected for a pure lengthening of plant cells without increase in their number. See *Declaration of Dr. Joel Sternheimer II dated October 26, 2001, Annexes 7a and 7b*.

In addition, fundings have recently been voted to a researcher at INSERM in Paris to perform controlled experiments on cell cultures, using inventor's patented technique.

Other experiences showing the utility of the invention are shown in Attachment B. See *Declaration of Dr. Sternheimer I dated May 19, 1999 at ¶ 6, Annex 2*.

As for the utility, it may be sufficient to note that a user contract has recently been signed (November 2, 2000) between Applicant and an Agricultural Research Institute in Japan. See *Declaration of Dr. Joel Sternheimer II dated October 26, 2001, Annex 9*.

Rejections Under 35 U.S.C. § 112 ¶ 2

Claims 1-8 and 11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The claims are vague, indefinite, incomplete, and incomprehensible.

Claim 1 has been replaced with new Claim 13. Set forth below is a discussion of

rejections (a)-(g) of Claim 1.

(a) The recitation of “associating with each amino acid a musical note whose frequency is transposed from the proper frequency of the amino acid” is vague, indefinite and incomprehensible because the proper frequencies of amino acid are not described. This is not the case for the following reasons:

- How the musical notes are “decoded and transposed: see Specification, page 8, line 12-page 9, line 21. The calculation was given in an earlier response (calculation array); it relies on the harmonic synchronization phenomenon predicted to occur within the cells between the amino acids frequencies when these lock on their respective tRNA within the time lapse of $10^{-12.5}$ s, similarly to many well-known frequency locking phenomena.
- How the man skilled in the Art can know that the decoding is correct: when it works and/or when it has been selected by a statistically significant number of patients presumably needing it (an unnecessary or incorrect decoding is normally rejected by the patient). *Declaration of Dr. Joel Sternheimer II dated October 26, 2001*, Annex B shows the proteins which have been selected by 10 patients or more of a single therapist, over a four year period (65 proteins out of a set of some 350 routinely used by this therapist). Similar testings are presently officially conducted in St. Marianna University School of Medicine at Kawasaki (Japan), where a new department is being constituted for this purpose.

(b) Claim 1 (b) (“determining the musical periods of said sequence of musical notes by identifying similar series of musical notes”) is incomprehensible when taken as a whole.

- How does one “spot” musical periods: See specification page 10, line 12-page 12, line 21 and examples: page 16, line 12-page 19, line 4 and page 20, line 4-page 21, line 29.

(c) The recitation of “the repartition” is incomplete because the term has no antecedent basis. This term has been eliminated from new Claim 13.

(d) Claim 1(c) (relates to determining tone quality) is incomprehensible when taken as a

whole. A modified form of determining tone quality is now in Claim 13(d).

(e) The recitation of "said musical sequence of said amino acid chain" (Claim 1) is incomplete because the phrase lacks antecedent basis. This rejection is now moot.

(f) The recitation of "tone quality" (claim 1) is vague and indefinite because the instant application fails to describe the derivation of a tone quality from a protein or a protein from a tone quality. To the contrary, the application does describe a tone quality. *See Specification at page 14, lines 12-14.*

(g) The recitation of "said musical sequence" is incomplete because the phrase has no antecedent basis. This rejection is now moot.

Rejections regarding Claim 2. Claim 2 has been cancelled and the step of Claim 2 is now step (c) of new Claim 13.

(h) The recitation of "rectifying individually said musical periods by adjusting the phrasing to the measure of said musical sequence" (Claim 2) is vague, indefinite, and incomprehensible.

(i) The recitation of "adjusting" (Claim 2) is vague, indefinite, and incomplete because the nature and degree of adjustment are not mentioned.

(j) Claim 2 is incomprehensible when taken as a whole.

To respond to items (h), (i) and (j), please note that the adjustment of phrasing to measure is what one does every time one must sing a text while following a rhythmic measure, for instance "Twinkle, twinkle little star how I wonder where you are", where the words "star" and "are" are longer to follow a regular rhythmic, so that the notes and melodic contours ("similar sequences of notes and signatures") match from one measure to the next, as explained in the specification.

Claim 3 has been canceled and no corresponding claim takes its place. Therefore, rejections (k) – (r) are moot.

The rejections of Claims 4-5 will now be discussed. Claims 4-5 have been replaced by new Claims 14-15.

(s) The recitation of "chromatic tempered scale" (Claims 4 and 5) is vague and

indefinite. The term is not defined. This expression corresponds to the definition given at the beginning of the description. English speaking people use preferably the expression “tempered scale,” “equal-tempered scale,” or “chromatic scale,” instead of “chromatic tempered scale,” but the meaning is the same. Reference is given at page 1, lines 4-5; the words “chromatic tempered scale” are used in the English summary of the cited paper; it designates the division of the octave in twelve equal intervals.

(t) The recitation of “said keynotes” (Claim 5) is incomplete because the term has no antecedent basis. This term has been omitted from new Claim 15; therefore this rejection is now moot.

(u) The recitation of “which are deduced ... with respect to central G” (Claim 5) is vague, indefinite, and incomprehensible. Said recitation means that any interval relative to the central G is replaced by the interval of opposite sign; for instance +2 semi-tones (for Q,K,E,M, relative to L,I,N,D) becomes 2 semi-tones, and so on.

Claim 7 has been cancelled and new Claim 16 takes its place.

(v) Claim 7 is incomprehensible when taken as a whole. *See Answer to Rejection (w)*.

(w) The recitation of “quantum vibrations associated to the mature protein after it is spatially folded back over itself” (Claim 7) is vague, indefinite, and incomplete because the instant application does not describe the properties of such vibration such that one of skill in the art can recognize or detect them. The quantum vibrations are the same as described earlier in the specification. *See, page 9, line 22 - to page 10, line 11*. However, they are transposed in a different way (being sealing waves of spatial type, as in reference quoted page 2, line 22 of the specification) according to the formula given to give color frequencies instead of sound frequencies. The information itself is no more temporal (in successive frequency intervals) but positional, *i.e.*, the respective position of colors corresponding to the amino acids positions in the usual 3-D representation of proteins, where every amino acid is represented by a little sphere, colored according to the code given in said claim.

(x) Claim 7 is vague and indefinite because the term “Argch” is undefined. The expression “Argch” has been replaced by its English equivalent “(cosh)⁻¹”. This rejection is now

moot.

Claim 8 has been replaced by new Claim 17. Response to the rejection of that claim is as follows:

(y) The recitation of “consists in the association to the different amino acids of the following colors” (Claim 8) is vague, indefinite, and incomprehensible. The meaning of the passage is not known. *See answer to rejection (w)*.

(z) The recitation of “Gly = dark red ...” (claim 8) is vague, indefinite, and incomprehensible. It is not known what is meant by the passage. *See answer to rejection (w)*.

Claims 9 and 11 have been cancelled. Therefore rejections (aa)-(bb) are moot.

Rejection Under 35 U.S.C. § 112 ¶ 1

Claims 1-8 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The examiner further states:

The claims are not enabled because the instant application does not disclose how to regulate protein synthesis. ... the application fails to measure or define the phase of protein elongation or to disclose to one of skill in the art how to recognize the phase of protein chain elongation. Additionally, it is not understood what is meant by a phase of protein chain elongation since it is well known that proteins are synthesized on polyribosomes... Hence, on a given nRNA, various growing nascent polypeptide chains are in various states of elongation and are presumably in different phases of elongation. Also, since there is more than one nRNA encoding a given polypeptide in a given cell, and since organisms are made of a large number of cells, it is reasonable to conclude that all possible stages of elongation of a given polypeptide exist at any one time. Thus, there would seem to be no “phase” to the elongation of any particular type of polypeptide chain in any particular organism. *Office Action of 5/25/01, page 6.*

A lot of available evidence contradicts this assumption. First, a periodicity is clearly visible on polyribosomes (See *Declaration of Dr. Joel Sternheimer II dated October 26, 2001*, Annex A of Attachment A, figure 1 from B. Alberts et al., *Molecular Biology of the Cell*,

Garland Publishing, New York and London, 3rd edition 1994, p. 238). Where there is a period, there is a phase.

Second, the existence of a phase in protein synthesis may be checked by comparison with the pauses in elongation as determined from accumulation of intermediate nascent chains of discrete sizes, which may be observed using gel electrophoresis such as in the work of S. Varenne et al. (J. Mol. Biol. 180, 549-576, 1984). In the example given in this paper on pFW 565 (E. Coli's outer membrane protein A), pauses may not only be seen to fit the musical "cadences" located as explained in patent application (note the average period of amino acids near the maximum amplitude, *i.e.*, maximum number of intermediate nascent chains).

The mere fact that they follow a regular pattern, as seen on figure 2 in contradistinction with the predictions of codon usage (which postulate that codon-anticodon binding follows a trial-and-error procedure, wherefrom pauses would simply be statistically correlated with rare codons, yielding a chaotic-like behavior), is by itself evidence of a phase, already in the case of bacteria, with "some" undetermined mechanism to control it – for which inventor's theoretically grounded scaling waves do provide an explanation (the theoretical papers are quoted in application, p. 1 and p.2).

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



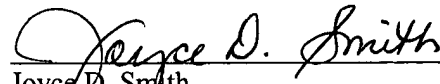
Ernest B. Lipscomb, III
Registration No. 24,733

In re: Joel Sternheimer
Appl. No.: 09/320,637
Filed: May 26, 1999
Page 12 of 12

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Charlotte Office (704) 444-1000
Fax Charlotte Office (704) 444-1111
CLT01/4495734v1

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on November 7, 2001.



Joyce D. Smith